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Asymmetric synthesis of nature inspired drug scaffolds: Applications of pluripotent building blocks

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Abstract

Natural products encompass a wealth of structural diversity within defined, nonplanar scaffolds; however, there are well-documented hurdles to their use in screening campaigns because of their limited availability relative to the quantities needed for structure activity relationship (SAR) development and clinical trials.[1] Thus, the recent decade has witnessed an upsurge in the development of privileged strategies for the de novo construction of nature-inspired compounds.[2] One such strategy represents the use of a single pluripotent functional group that can be decorated through reactions with variety of reagents, thereby empowering the synthesis of skeletally diverse compound collections with high 3D-content.[3] On the other side, multicomponent reactions (MCRs) hold a privileged position in diversity oriented synthesis (DOS), allowing the formation of many new bonds and bringing together more than two reactants in one-step. A particularly attractive DOS strategy, is a reaction that combines both strategies in one. Such a strategy should produce a large set of stereochemically diverse molecular scaffolds, not achievable by either strategy alone. In fact, the design and synthesis of a quality compound library containing a skeletally diverse scaffolds, whose members rapidly deliver new chemical probes active against multiple phenotypes, is paramount in drug discovery. In this context, within our group, we have developed several starting material- and MCR-based DOS approaches utilizing few pluripotent building blocks. Gratifyingly, the developed libraries offered potential biological activities on different disease states.

Biography:

Srinivasulu received his B.Sc and M.Sc degrees from Sri Venkateswara University in 2006 and 2008, and his PhD from CSIR-IICT (India) in 2013. He joined GVK Bio-Sciences Pharma Company as a Senior Research Associate in 2014. Srinivasulu carried out his Postdoctoral research at UNIST, South Korea in 2015, and now at RIHMS, University of Sharjah, UAE. He secured first rank in his M.Sc (medicinal chemistry) and awarded CSIR-JRF scholarship for his doctoral research. His research interests include development of Novel organic methodologies, Asymmetric synthesis, Medicinal chemistry and Nano-catalysis. He has published more than 25 papers in reputed international journals which includes nature, ACS, RSC and wiley publishers.

Speaker Publications:

1. "Multidirectional desymmetrization of pluripotent building block en route to diastereoselective synthesis of complex nature-inspired scaffolds' Nature Communications volume 9, Article number: 4989 (2018)

2." Sequencing [4 + 1]-Cycloaddition and Aza-Michael Addition Reactions: A Diastereoselective Cascade for the Rapid Access of Pyrido[2′,1′:2,3]/Thiazolo[2′,3′:2,3]imidazo[1,5-a]quinolone Scaffolds as Potential Antibacterial and Anticancer Motifs; J. Org. Chem. 2019, 84, 22, 14476–14486 Publication Date:October 21, 2019

3. Divergent Strategy for Diastereocontrolled Synthesis of Small- and Medium-Ring Architectures; J. Org. Chem. 2020, 85, 16, 10695–10708 Publication Date:July 29, 2020

4. Modular Bi-Directional One-Pot Strategies for the Diastereoselective Synthesis of Structurally Diverse Collections of Constrained β-Carboline-Benzoxazepines; Volume23, Issue57 October 12, 2017 Pages 14182-14192

5. Multidirectional desymmetrization of pluripotent building block en route to diastereoselective synthesis of complex nature-inspired scaffolds; PMID: 30478283

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